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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,573	07/11/2003	Ellen Filvaroff	P1381R1C1P4C1	8245

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
02/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/617,573	FILVAROFF ET AL.	
	Examiner	Art Unit	
	DONG JIANG	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61,63-66,68,69,76-84 and 86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61,63-66,68,69,76-84 and 86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/24/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's response filed on 27 October 2008 is acknowledged and entered.

Currently, claims 61, 63-66, 68, 69, 76-84 and 86 are pending and under consideration.

Information Disclosure Statement

The information disclosure statement filed 11/24/08 is acknowledged, and has been considered. A signed copy is attached hereto.

Withdrawal of Objections and Rejections:

The prior art rejection of claims 61, 63, 64, 76 and 77 under 35 U.S.C. 103(a) as being unpatentable over Medlock et al. (US7,094,566 B2) is withdrawn in view of applicant's argument.

Applicants argue, on pages 4-5 of the response, that the present application claims priority to the U.S. provisional application 60/175,481 ('481) filed on 1/11/00 (see amendment filed on 1/16/07), which predates the Medlock reference (with the effective filing date of 3/16/00), and provides sufficient support for the currently claimed subject matter (for example, Example 7, and at page 66, lines 17-21). Application '481 teaches that anti-PRO10272 antibodies can be used to counteract proinflammatory activity of the polypeptide, and thus may be therapeutically useful in the treatment of various inflammatory diseases, or certain autoimmune disorders such as *rheumatoid arthritis* and multiple sclerosis; and that the antibodies may also be useful in neutralizing its osteoclatogenic activity in various bone disorders involving bone resorption (page 66). As such, applicants argument is persuasive, and the rejection of above mentioned claims is withdrawn.

All other prior art rejections made in the last Office Action are withdrawn in view of applicant's argument (see above).

Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61, 63-66, 68, 69, 76-84 and 86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a method of treating a degenerative cartilaginous disorder *associated with* the polypeptide of SEQ ID NO:6 using an antagonist antibody thereto, does not reasonably provide enablement for claims to a method of treating any or all degenerative cartilaginous disorders (regardless of the cause) using said antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The present claims are directed to a method of treating a degenerative cartilaginous disorder with an antagonist antibody binding to the polypeptide of SEQ ID NO:6 (claim 61, for example) or a variant thereof (claim 76, for example), which read on a method of treating any or all degenerative cartilaginous disorders using said antibody. However, while the specification teaches that the polypeptide of SEQ ID NO:6 (PRO10272, or IL-17E) induces production of IL-8 and IL-6, proinflammatory molecules (page 130, line 27, and page 136, lines 19-20), and likely contribute to loss of articular cartilage in arthritic joints (page 138, the last line), it does not teach that IL-17E is involved in any or all degenerative cartilaginous disorders. Further, the prior art has not established such either. Although IL-6 and IL-8 are known potent proinflammatory cytokines, prior art has revealed that they can be induced or upregulated by multiple factors. For example, Chaly et al. (Cytokine, June 2000, 12(6):636-43) teaches that TNF-α and IL-1 are the most powerful inducers of IL-8, and other molecules such as SAC (Staphylococcus aureus Cowan 1) and LPS also stimulate IL-8 expression (the abstract). Further, Xiong et al. (J. Interferon Cytokine Res., July 2001, 21(7):529-37) teaches that nitric oxide (NO) mediates upregulation of IL-

8 in human pancreatic cancer cells (the abstract). Furthermore, the instant application also teaches that, besides IL-17E, other family members such as IL-17, IL-17C and IL-17F can induce the production of IL-6 and IL-8 (page 138, the last line, and page 142, line 20). Therefore, induction of IL-6 and IL-8 are not IL-17E-specific, and it can be promoted by a number of factors other than IL-17E and/or or IL-17 family members depending upon different pathological conditions. Some of degenerative cartilaginous disorders may not relate to IL-17E and/or IL-17 family at all. As such, those conditions not involving IL-17E would not be treatable with an antagonist antibody to IL-17E. It would not be unpredictable as to what degenerative cartilaginous disorders, other than those showing the involvement of IL-17E, should be treated with the claimed method without undue experimentation.

Due to the large quantity of experimentation necessary to determine whether IL-17E (PRO10272 of SEQ ID NO:6) is involved in any or all degenerative cartilaginous disorders; the lack of direction/guidance presented in the specification regarding same; the absence of working examples directed to same; the complex and unpredictable nature of the invention; the state of the prior art that has established that IL-6 and IL-8 can be induced or upregulated by a number of factors besides IL-17E, and that has not established that any or all degenerative cartilaginous disorders are associated with IL-17E, and the breadth of the claims which encompass any or all degenerative cartilaginous disorders, undue experimentation would be required of the skilled artisan to use the claimed invention in its full scope.

Claims 76-83 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The independent claim 76 is directed to a method of treating a degenerative cartilaginous disorder with an antagonist antibody binding to a variant of the polypeptide of SEQ ID NO:6 (at least 85% sequence identity). To an extent the claim encompasses antibodies that bind to epitopes not found in the particularly disclosed sequence.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The limitations of present claim 76 encompasses significant structural dissimilarity of the polypeptide as compared to the disclosed SEQ ID NO:6. The instant specification merely discloses *one* amino acid sequence of SEQ ID NO:6, and no other variants or epitopes thereof or antibodies thereto meeting the limitations of these claims were ever identified or particularly described, and no sequence variations have been shown to correlate with the biological activity required by the claim. Thus, with the exception of the polypeptide of SEQ ID NO:6 and antibodies thereto, the skilled artisan cannot envision the detailed chemical structure of the encompassed % variants. Therefore, the specification does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the % variants of the polypeptide of SEQ ID NO:6, the epitopes not found in SEQ ID NO:6, or the antibodies thereto.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

The Office, therefore, concludes that SEQ ID NO:6, by itself , is not representative of all variants encompassed in claim 76, and that to the extent those variants might possess epitopes not found on the disclosed polypeptide, and antibodies to such epitopes have not been described. With the exception of the antibody to the polypeptide of SEQ ID NO:6, no other antibody to the variants of SEQ ID NO:6 meets the written description provision of 35 U.S.C. §112, first

paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 65, 66, 78 and 79 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Medlock et al., US7,094,566 B2, for the reasons of record set forth in the last Office Action mailed on 8/8/08, at pages 3-4.

Applicants argument filed on 27 October 2008 has been fully considered, but is not deemed persuasive for the reasons below.

At pages 4-5 of the response, the applicant argues that the present application claims priority to the U.S. provisional application 60/175,481 ('481) filed on 1/11/00 (see amendment filed on 1/16/07), which predates the Medlock reference (with the effective filing date of 3/16/00), and provides sufficient support for the currently claimed subject matter (for example, Example 7, and at page 66, lines 17-21). This argument is not persuasive for the following reasons. While application '481 teaches that anti-PRO10272 antibodies can be used to counteract proinflammatory activity of the polypeptide, and thus may be therapeutically useful in the treatment of various inflammatory diseases, or certain autoimmune disorders such as

rheumatoid arthritis and multiple sclerosis; and that the antibodies may also be useful in neutralizing its osteoclatogenic activity in various bone disorders involving bone resorption (page 68, lines 15-19); it does not specifically teach the treatment of osteoarthritis and psoriatic arthritis with anti-PRO10272 antibodies. In fact, application '481 teaches the opposite with this regard, i.e., it teaches that the polypeptide of PRO10272 (not the antibody thereto) may be useful in the treatment of psoriasis (page 56, lines 12-14), and in promoting bone and cartilage growth, for example, in the treatment of osteoporosis and *osteoarthritis*, or in stimulating regeneration of dentin/bone lost due to periodontal disease (page 56, lines 16-18). Therefore, contrary to applicants argument, the provisional application 60/175,481 does not provide any support for the subject matter in claims 65, 66, 78 and 79. The prior art rejection of these claims is maintained.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on 9:30 am - 7:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dong Jiang/
Primary Examiner, Art Unit 1646
1/30/09